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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/986,606	12/08/1997	NATHAN H. SLAONE	21578-013RCE	5146

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EXAMINER	
LUKTON, DAVID	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 01/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	08/986,606	SLAONE, NATHAN H.	
	Examin r	Art Unit	
	David Lukton	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-9 and 15-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-9 and 15-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Pursuant to the directives of the amendment filed 9/4/03, claims 10-14 have been cancelled, claims 4-8, 15 amended, and claims 16-18 added. Claims 4-9, 15-18 are pending.

Applicants' arguments filed 9/4/03 have been considered and found not persuasive.

A substitute specification has been submitted (filed 9/4/03). However, this will not be entered, because of the introduction of new matter, as explained below.

*

The amendment filed 9/4/03 is objected to under 35 U.S.C. §132 because it introduces new matter into the specification. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The amendment requests that the N-terminal amino acid be changed from pyroglutamic acid to glutamic acid. (This may be found on page 2, line 7 of the new specification). There is no evidence that this was an inadvertent error; moreover, in applicants publication (*Cytokine* 8, 1-5, 1996), this matter of pyroGlu *versus* Glu is discussed, e.g., at page 3, col 2.

Applicant is required to cancel the new matter in the response to this Office Action.

*

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-9, 15-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Each of the cited claims is drawn to a peptide or composition or method. In each case, the claim is drawn to a peptide which comprises SEQ ID NO:1. There may be support in the specification for a peptide that consists of SEQ ID NO:1, but it does not appear that support exists for a peptide that comprises SEQ ID NO:1. Applicant is requested to point to the location in the text where support for this may be found.

In response to the foregoing, applicants have pointed to various pages and line numbers of the originally filed application. First, it is assumed that by "page 2" is really meant "page 3" according to the original numbering of the pages. Second, the lines are not numbered, and so it is not possible to determine exactly what passages are being referred to. Third, even allowing for a significant "margin of error" in the counting of line numbers, the cited passages do not state what applicants have asserted that they state. It may be true that one can infer that at the time of filing, applicants were in possession of both SEQ ID NO: 1, and a full length protein that has been termed "ANUP". But the fact that applicants may have been in possession of the full length "ANUP" does not, in any way, provide support for the term comprises. As indicated above, the switch from pyroGlu to Glu

constitutes new matter. But setting aside this issue for the moment, the specification as filed provided support for the following (the switch from pGlu to Glu is made for purposes of discussion only):

ELKCYTCKEPMTSAAC

In addition, one could perhaps infer that this peptide was somehow obtained from a larger peptide which as been assigned the designation "ANUP". First, even if the N-terminal amino acid had been Glu rather than pGlu, the implication was that the 16 AA sequence above was the N-terminal sequence, and that no amino acid or peptide could be bonded to the N-terminus of the 16 AA sequence. Further, the requirement for pGlu at the N-terminus reinforces this conclusion. Now, the claims permit any amino acid or peptide to be bonded to the N-terminus; this is permitted by the term "comprises". Thus, peptides such as the following would now be encompassed (wherein each "Xn" represents an amino acid):

X1-X2-E-L-K-C-Y-T-C-K-E-P-M-T-S-A-A-C

X1-X2-X3-X4-X5-E-L-K-C-Y-T-C-K-E-P-M-T-S-A-A-C

X1-X2-X3-X4-X5-X6-X7-X8-X9-E-L-K-C-Y-T-C-K-E-P-M-T-S-A-A-C

None of this is supported by the specification as filed. In addition, the claims would permit any number of amino acids to be bonded to the C-terminus. Accordingly, peptides such as the following would now be encompassed:

X1-X2-X3-X4-X5-E-L-K-C-Y-T-C-K-E-P-M-T-S-A-A-C-X11-X12-X13-X14-X15-X16

Third, the term "comprises" would also encompass the possibility of adding substituents to side chains of amino acids. This would include, for example, acetylation of a lysine side chain, or benzylation of a cysteine side chain. None of this was in any way suggested by the specification as filed.

None of the passages recited by applicants support the term "comprises". In addition, a few of the cited passages have nothing to do with the issue raised by the examiner. It is suggested that the term at issue be deleted. The issues discussed above with respect to the term "comprises" apply as well to claims that recite the term "consisting essentially of" (e.g., claims 16-18).

An issue separate from the foregoing pertains to the phrase "a composition comprising" in reference to SEQ ID NO: 1. Applicants are requested to identify the specific passage where support can be found. Given the ambiguity surrounding page numbers and line numbers, the passage should be identified in a manner that is very clear and unambiguous. Merely citing page and line numbers does not qualify as "clear and ambiguous" in the instant case. It is stipulated that there may exist one or two examples of compositions that contain the peptide of SEQ ID NO: 1 (with pGlu as the N-terminal amino acid, rather than Glu). However, this does not constitute descriptive support for any and all "compositions" that contain the peptide in question. Applicants appear to be of the view that if a specification provides one or two examples of species, this somehow amounts to a description of a genus. However, applicants are not correct on this point. Consider,

for example, the following:

- In *In re Smith* 173 USPQ 679, 1972 pertained to an emulsion coating composition in which a pigment is coated with an organic compound. The court found that a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads. In the instant case the "genus" could be viewed as original claim 1, and the subgenus current claim 20. In the instant case, claim 20 has been fashioned on the basis of the original genus, together with six (or perhaps seven) species. As with the Smith case, these six peptide species do not amount to a description of the claimed genus.

- *Tronzo v. Biomet* (47 USPQ2d at 1829 1998) pertained to what is now USP 4,743,262, in which the claims are drawn to an acetabular cup prothesis. The issue concerned written description of a priority document, which is closely allied with the issue of new matter. The court found that claims to a generic cup shape were not entitled to filing date of parent application which disclosed only a conical cup. Thus, one could conclude that an extrapolation from a specie to a genus would constitute new matter.

- The claims in *In re Sus* (134 USPQ 301 1962) were drawn to light-sensitive aryl azides. The issue was whether the structural formula recited in the claims (especially the term "substituted aryl") was adequately supported by a general description of the claimed invention, together with the disclosure of several species. The court found that the claimed genus was not adequately described by disclosure of several species, even when taken together with a general description of the claimed invention. Such is the case here. An attempt has been made in the instant case to create a genus which shares a few of the features of several species. Such an extrapolation constitutes new matter.

Clearly, one or two examples of species does not amount to a description of a genus. It is suggested that applicants (a) claim a peptide that consists of SEQ ID NO: 1, and (b) submit a new sequence listing in which the terminal amino acid is specified to be pGlu.

Another issue concerns claim 5. This claim stipulates that it is possible for a peptide to

comprise a "concentration" of a peptide. This is physically impossible, although that is not the point. The point is that there is no description for this in the specification. Applicants are requested to identify the specific passage where support can be found. Given the ambiguity surrounding page numbers and line numbers, the passage should be identified in a manner that is very clear and unambiguous. Merely citing page and line numbers does not qualify as "clear and ambiguous" in the instant case.

Another issue concerns claim 6. This claim asserts that the peptide is activated by contacting with any and all detergents. While there may be some support for using SDS in this regard, but it does not appear that there is descriptive support for any other detergent, or for detergents in general. Applicant is requested to point to the location in the text where support for this may be found. Given the ambiguity surrounding page numbers and line numbers, the passage should be identified in a manner that is very clear and unambiguous. Merely citing page and line numbers does not qualify as "clear and ambiguous" in the instant case.

Another issue concerns the recitation of SEQ ID NO: 1 in the claims. This constitutes new matter because of the presence of the pyroGlu residue at the N-terminus.

*

The following is a quotation of the first paragraph of 35 U.S.C. §112:

The specification shall contain a written description of the invention, and of the manner and process of

> making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8, 9, 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The cited claims are drawn to a method of killing a tumor cell. These claims encompass killing both *in vitro* and *in vivo*. However, enablement is lacking, at least for the case of achieving the "contacting" by administering the peptide to a tumor-bearing mammal.

As stated in *Ex parte Forman* (230 USPQ 546, 1986) and *In re Wands* (8 USPQ2d 1400, Fed. Cir., 1988), the factors to consider in evaluating the need (or absence of need) for "undue experimentation" are the following: quantity of experimentation necessary, amount of direction or guidance presented, presence or absence of working examples, nature of the invention, state of the prior art, relative skill of those in that art, predictability or unpredictability of the art, and breadth of the claims. The following references discuss the matter of various attempts by oncologists to treat cancer: Viallet (*Lung Cancer* **15** (3) 367-73, 1996); Kemeny (*Seminars in Oncology* **21** (4 Suppl 7) 67-75, 1994); Newton (*Expert Opinion on Investigational Drugs* **9** (12) 2815-29, 2000); Giese (*Journal of Cancer Research and Clinical Oncology* **127** (4) 217-25, 2001); Garattini (*European Journal of Cancer* **37** Suppl 8 S128-47, 2001); Ragnhammar (*Acta Oncologica* **40** (2-3) 282-308,

2001).

As is evident, attempts to kill cancer cells in tumor-bearing mammals using agents which have exhibited *in vitro* activity leads to "unpredictable" results. In addition, applicant has made an admission (page 5, lines 1-2) that the peptide failed to kill tumor cells when SDS was absent.

In response to the foregoing, applicants have argued that they have amended claims 8 and 9 in accordance with what the examiner suggested. However, applicants are not correct. Claim 8 encompasses "killing" *in vivo*, whereas in the proposed claim, "killing" *in vivo* was excluded. Accordingly, claim 8 remains rejected. Applicants have also asserted that they have submitted a declaration demonstrating in vivo efficacy of SEQ ID NO: 1 in nude mice. However, no such declaration has been received. It is suggested that the declaration be resubmitted.

*

Claims 5 and 15-17 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 5 is drawn to a polypeptide that comprises a specified concentration of a polypeptide. Applicants are requested to explain what this means in physical terms. For example, suppose that one has a 5 mL vial which contains 1 gram of a purified peptide of SEQ ID NO: 1. In reality, the "concentration" of the peptide would be a meaningless parameter since the peptide is the only compound present in the vial (apart from some air). But in applicants opinion, what exactly would be the "concentration" of the peptide in this vial?

- Claim 15 recites (last line) that apoptosis can be promoted "in" a tumor cell. It appears that the preposition "of" is intended instead.

- Each of claims 16 and 17 is drawn to a composition. A "composition", however, must have at least two components. (Note that even claim 17 doesn't specify a second component). That is to say, a pure peptide is a compound, not a composition, but a peptide in combination with at least one other compound would be a composition. By using the term "composition", each of claims 16 and 17 mandates the presence of a second component, but without giving any indication of what that second component is. Is the second component a pharmaceutically acceptable carrier? Is the second component a detergent? Is the second component another peptide? If the term "composition" is supported by the description (and it probably isn't), the second component should be specified. New matter, of course, must be avoided.

*

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 703-308-3213. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached at (703) 308-2923. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

D. Lukton

DAVID LUKTON
PATENT EXAMINER
GROUP 1600